

Pharmacotherapy for Hoarding Disorder: How did the Picture Change since its Excision from OCD?

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Abstract. This brief review deals with the various issues that contributed to the creation of the new Diagnostic and Statistical Manual condition of hoarding disorder (HD) and attempts at reviewing its pharmacotherapy. It appears that after the newly founded diagnosis appeared in the literature as an autonomous entity, distinct from obsessive-compulsive disorder, drug trials are not being conducted and the disorder is left in the hands of psychotherapists, who on their part, report fair results in some core dimensions of HD. The few trials on HD specifically regard the serotonin-noradrenaline reuptake inhibitor venlafaxine, and, possibly due to the suggestion of a common biological background of HD with attention-deficit/hyperactivity disorder, the psychostimulant methylphenidate and the noradrenaline reuptake inhibitor atomoxetine. For all these drugs, positive results have been reported, but the evidence level of these studies is low, due to small samples and non-blind designs. Regrettably, there are currently no future studies aiming at seriously testing drugs in HD.

ARTICLE HISTORY

Received: October 26, 2018
Revised: December 21, 2018
Accepted: January 17, 2019

DOI:
10.2174/1570159X17666190124153048

Keywords: Hoarding disorder, obsessive-compulsive disorder, drug treatment, cognitive-behavioural therapy, atomoxetine, methylphenidate, venlafaxine.

1. INTRODUCTION

Hoarding disorder (HD) is a recently emerged diagnosis. Until the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-5) [1], HD was embedded in the diagnosis of obsessive-compulsive disorder (OCD) and within the anxiety disorders [2]. However, since the first-second decades of the 21st Century, there were strong indications for HD as a brand new DSM category, based on psychopathological [3-6], epidemiological [7], neuropsychological [8-10], and neuroimaging [11] data.

2. DEFINING HD: BORDERS AND DIMENSIONS

HD is now part of the DSM-5 [1] obsessive-compulsive (OC) and related disorders, which include, among others,

obsessive-compulsive disorder (OCD), body dysmorphic disorder (BDD), trichotillomania, and excoriation disorder. HD is characterized by “persistent difficulty discarding or parting with possessions, regardless of their actual value, as a result of a strong perceived need to save the items and the distress associated with discarding them” [1]. Six criteria define the diagnosis of HD, which, in 80-90% of cases, is accompanied by excessive buying, collecting and/or stealing items (something that puts HD side-by-side with other impulse control disorders). Hoarded items are unnecessary or have no sufficient space available. Individuals with HD may have different degrees of insight, from absent to fair/good.

HD must be distinguished from normal collecting, which is common among the population. From an evolutionary perspective, the tendency to collect objects can be regarded as adaptive, granting survival when there is dearth of resources [12, 13]. According to a cross-sectional study, children begin to gather and store their possessions from about two years of age and this behaviour peaks until about age six, when almost 70% of normal children display this trait [14]. Normal collectors differ from hoarders as they display

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minimal clutter and impairment, and more focusing, selectivity, and ability to classify accumulated objects [15]. The key characteristic that differentiates hoarding as behaviour from hoarding as a clinical entity is that the latter results in the accumulation of a large number of possessions that cover and clutter the living areas of the house, impairing their use [3]. The observation that collecting behaviour can become pathological in patients with specific patterns of brain damage led researchers to hypothesise that a cognitive dysfunction affecting the prefrontal areas in charge of mediating decision-making, attention, and emotional regulation could account for abnormal collecting. Indeed, there is recent evidence for a unique increase in prefrontal grey matter volume (Brodmann areas 10 and 11) in HD, compared to OCD and healthy controls [16]. This neurobiological abnormality may relate to the pathophysiology of HD. Furthermore, HD and OCD display different activation patterns during Go/NoGo task performance, in that HD patients hyperactivate the right precentral gyrus with correct rejects, while OCD patients hyperactivate the right orbitofrontal cortex; with commission errors, only OCD patients hyperactivate bilaterally their orbitofrontal cortex [11].

The disorder is also partly familial, with half of HD patients having a relative who also hoards. Twin studies indicate that heritability is moderate-to-high, with about 50% of the variability in hoarding behaviour attributable to genetic factors. Environmental factors mainly have a time-specific effect, accounting for the change of hoarding symptoms during the different life phases [17].

In the 1990s, Frost and colleagues developed a cognitive-behavioural model of hoarding [18]. They underlined the complex relationship between: (a) core dimensions, *i.e.*, acquiring, clutter, and difficulty discarding; (b) information-processing deficits in the fields of decision-making, categorization/organization, and memory; (c) maladaptive beliefs regarding the need to keep control over possessions, the responsibility for possessions, and the necessity of perfection; (d) behavioural avoidance; (e) emotional attachment. Apparently, all these factors lead to pathological hoarding. The three domains of acquiring, clutter, and difficulty in discarding appear to constitute a cross-cultural phenomenon, having been encountered, besides the US and Europe, also in China [19].

3. ANIMAL HOARDING: ANOTHER CATEGORY?

A peculiar form of HD is animal hoarding, which is described as the “accumulation of a large number of animals and a failure to provide minimal standards of nutrition, sanitation, and veterinary care and to act on the deteriorating condition of the animals (*e.g.*, disease, starvation, or death) and the environment (*e.g.*, severe overcrowding, extremely unsanitary conditions)” [1]. The mean number of animals per hoarder is about 40 [20]. Animal hoarding has been suggested to be a distinct nosological entity, since the insight is significantly impaired, the sanitary conditions are poorer than in object hoarding, and there is an affectional bond with hoarded animals [20], even if an excessive emotional attachment (“hypersentimentality”) to apparently worthless inanimate objects has also been noted in animal hoarding [21, 22].

4. EPIDEMIOLOGY ISSUES

The prevalence of HD is relatively high in nationally representative samples, ranging from 1.5% to 6% of the population [7, 23]. A number of epidemiological studies have found a greater prevalence among males, whereas, in clinical samples, patients are predominantly female [1]. Hoarding symptoms are thrice as common in older adults (age range 55-94 years) than in younger adults (age range 34-44 years) [24]. A reason could lie in the age of onset of HD; while the mean age of onset for symptoms is between 10-20 years and the mean age of onset for possible HD diagnosis is between 20-30 years, one-fourth of older adults with HD report a possible onset after the age of 40. Moreover, HD symptoms worsen over time, causing increasing impairment, thus most study samples consist of elderly patients [25].

5. CLINICAL AND SOCIAL ISSUES

HD is often accompanied by symptoms such as perfectionism, indecision, distractibility, and procrastination [7]. As shown by a large-scale study, comorbidity with other disorders is very common, with approximately 75% of HD patients having a mood or anxiety disorder other than OCD [26]. The most common comorbid conditions are major depressive disorder (MDD), social anxiety disorder (SAD, also known as social phobia), and generalised anxiety disorder (GAD). The early observation that inattention appeared to be a core characteristic of HD patients pointed to a common biological background for HD and attention deficit/hyperactivity disorder (ADHD) [27]. In fact, more than 20% of HD patients had comorbid ADHD, while fewer than 20% of HD patients had OCD comorbidity; furthermore, only 3% of the latter had ADHD comorbidity [26]. It has been suggested that inattentiveness and impulsivity/compulsivity dimensions are two core characteristics of HD [28]. This hypothesis originates from the observation that patients with HD often shift attention from an item to another, with subsequent difficulties in making decisions during sorting tasks [12, 29]. Additionally, attentional symptoms can predict hoarding severity [27]. Moreover, a cross-sectional survey showed childhood inattention, not hyperactivity, to be associated with lifetime hoarding symptoms [30] and a recent family study showed a common load for inattentive features and hoarding [31]. HD patients may also have acquisition-related impulse control disorders (*i.e.*, compulsive buying, kleptomania, and acquiring items) [32-34].

HD may lead to functional consequences. Severe clutter interferes with basic activities, such as walking throughout the house, cooking, cleaning, personal hygiene, and even sleeping. Domestic devices may be broken, and utilities like electricity, gas, and water may be disconnected, as access to repair work may be problematic [35]. In most severe cases, HD can cause public health and legal issues, putting patients at risk for injuries due to fire, falling (especially aged people), and poor sanitation, which have a great impact not only on the patients themselves and their family, but also on neighbours. HD is associated with occupational impairment, poor quality of family relationships, and frequent conflict with neighbours and local authorities, with some patients getting involved in legal eviction processes [36].

HD represents one of the few new diagnoses included in the DSM-5. In the past, it was linked with OCD or even considered a subtype of OCD, yet it is not directly mentioned in the DSM-IV-TR [37] or in 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) [38] as part of OCD, in the chapter of Anxiety Disorders. In the DSM-IV-TR, the main features of HD were listed as one of the eight diagnostic criteria for the obsessive-compulsive personality disorder (OCPD). Whether hoarding as part of OCPD differs from hoarding as part of OCD has remained largely unclear. One potential difference is in whether hoarding behaviour is seen as part of one's character (OCPD) or recognised as disproportionate (OCD) [39]. Hoarding behaviour has been described in several organic and mental disorders with different connotations, such as obsessions or compulsions in OCD, loss of energy in major depressive disorder (MDD), delusions in schizophrenia spectrum or other psychotic disorders, restricted interests in autism spectrum disorder (ASD), and cognitive deficits in major neurocognitive disorders [40, 41]. With the publication of the DSM-5, HD has become a separate diagnostic category. In the description of the differential diagnosis between OCPD and OCD, the DSM-IV-TR states that “a diagnosis of OCD should be considered especially when hoarding is extreme (e.g., accumulated stacks of worthless objects present a fire hazard and make it difficult for others to walk through the house)”. Hence, the DSM-IV-TR considers that hoarding can be a symptom of severe OCD, differently from any of the previous editions of the DSM [3, 5, 37]. While there is no doubt that hoarding in OCD can be secondary to obsessive fears, such as difficulties discarding items for concern of contaminating or harming others, or to compulsions, with the need to perform checking rituals before discarding any item [42], the accumulating evidence points to the fact that hoarding symptoms are not frequently associated with OCD. Although 5-10% of OCD patients show hoarding symptoms, more than 80% of HD patients do not have other OCD symptoms [5, 26, 42]. Additionally, advances in research show significant differences between HD and OCD in aspects related to genetics, phenomenology, degree of insight, clinical course, treatment response, and cognitive, behavioural, and emotional correlates. This led to the conclusion that the two are distinct disorders [3, 41, 43-45]. As a consequence, the DSM-5 Obsessive Compulsive Spectrum Sub-Work Group of the Anxiety, Obsessive-Compulsive Spectrum, Posttraumatic, and Dissociative Disorders Work Group decided to recommend the creation of the new diagnostic category HD [3,4], part of the chapter of Obsessive-Compulsive Spectrum Disorders of the DSM-5 [46]. It also suggested to remove the hoarding criterion of OCPD [3]. The inclusion of HD as a separate diagnosis potentially increased the usefulness of the nosological system and improved clinical utility by enhancing public awareness and increasing case identification, diagnostic accuracy, and tailoring of treatment. It is considered well accepted and perceived as non-stigmatising by its sufferers and clinicians dealing with it [3, 47]. However, hoarding remains largely unrecognised and undertreated, perhaps also because it is underreported [48].

6. THE SPLIT OF HD FROM OCD ENSUED IN DIVERSIFIED TREATMENT

HD is considered a fairly treatment-resistant disorder and currently there are no recognised professional guidelines for its management. Dealing with pathological hoarding within OCD has generally involved serotonin-reuptake inhibitors (SSRIs) and/or cognitive-behavioural treatment (CBT). Similar treatment modalities have been used for pathological hoarding that does not occur as part of OCD. Research suggests that compulsive hoarding is a predictor of treatment dropout, failure, or worse outcome in drug and behavioural treatment of OCD [49]. Anyway, the available literature on the treatment of hoarding reports mixed results [50]. The presence of hoarding symptoms in OCD patients was found to constitute the strongest predictor of non-response to medications or CBT in one study [51]. Another study observed only limited improvement in OCD patients for whom hoarding was one of the symptoms [52]. Similar results were reached by two studies by the same working group, which investigated the efficacy of citalopram and escitalopram in OCD patients with hoarding symptoms [53, 54]. A recent meta-analysis showed that patients with OCD and prominent hoarding were half as likely to respond to either pharmacological or behavioural therapy compared to patients with OCD and symptoms other than hoarding [55]. On the other hand, five studies found treatment response in OCD patients to be unaffected by hoarding symptoms [56-60]. In addition, a large study comparing hoarding OCD patients with non-hoarding OCD patients found that a comparable proportion of patients in the two groups reported moderate response or total remission with SSRIs, as well as with CBT [61]. Thus, hoarding should not be considered a constant predictor of poor response to SSRIs. A recent meta-analytic study examined the response of pathological hoarding – irrespective of whether it occurred in the context of OCD – to pharmacological agents, by assessing seven trials [62]. Included agents were SSRIs; serotonin- and noradrenaline-reuptake inhibitors (SNRIs), more specifically venlafaxine; augmentation of SSRIs with the atypical antipsychotic quetiapine; methylphenidate (MPH); the tetracycline antibiotic minocycline, which has been tested in an open-label trial as augmentation to SSRIs in OCD [63]; and the opioid antagonist naltrexone. About half of the patients treated with pharmacotherapy responded [62]. The study supports the use of SSRIs in HD patients, but also encourages to perform further pharmacotherapy studies for pathological hoarding as they are still scanty. A prospective study measured response to paroxetine administered for 12 weeks in compulsive hoarders; they responded with a mean 31% decrease in symptom severity, similarly to non-hoarding OCD patients, however the medication was not well tolerated, with the most common side effects being the anticholinergic ones, such as fatigue, sedation, constipation, headaches, and decreased libido [64]. This could have depended from the study sample being mostly represented by middle-aged women, for whom these effects can be more problematic [41]. The few case reports that tested the atypical antipsychotics risperidone and quetiapine in HD suggested very limited benefit [65]. A randomised double-blind, cross-over, placebo-controlled trial investigated

the effect of naltrexone augmentation to SSRIs in OCD patients who had not responded to adequate doses of SSRIs or clomipramine for at least two months [66]. Participants underwent 5 weeks of treatment with naltrexone, with a lack of OC symptom improvement. This could be due to either ceiling effect or alternatively, to a non-specific exacerbation of depression and anxiety, but does not appear to depend on OC symptoms [66].

Summarising, it is unclear whether the presence of hoarding symptoms in OCD confers treatment resistance and it appears that standard anti-OCD drug treatment could be useful for hoarding symptoms. However, the above trials were conducted on OCD populations, rather than on pure HD or specifically on HD patients. What one could have expected after the diversification of the two disorders is that some studies could test the effects of standard anti-OCD medication in HD, but it has not been so. After the diagnostic/nosographic split, few studies have been conducted on HD-only populations, despite HD prevalence is about the same as OCD. A recent open-label trial showed that extended-release venlafaxine administered for 12 weeks significantly decreased hoarding symptom severity in adults with HD (mean age: 51.8 years) [67]. Unfortunately for aged people with HD, who represent a considerable portion of HD-diagnosed people, age was negatively correlated with improvement in hoarding symptom severity, hence venlafaxine may be ineffective in older adults with HD.

Due to the conjecture that inattention and impulsivity-compulsivity could represent two other core aspects of hoarding symptomatology, two studies investigated the efficacy of ADHD medications in HD. The first was a case series of methylphenidate in four HD SSRI/SNRI-resistant patients, who reacted well to treatment and showed improved responses on the continuous performance test [68]. However, after this suggestion, no randomised-controlled trial (RCT) followed. Another trial involved a drug more specifically used for the mainly inattentive subtype of ADHD, atomoxetine, by targeting attentional and inhibitory control networks [69]. Six patients were complete responders and three partial responders to flexible drug dosages (40-80 mg) for 12 weeks. Inattentiveness and impulsiveness showed a significant mean score drop of 18.5% from baseline to the endpoint. The improvement of hoarding symptoms correlated with reduced patient disability and increased global functioning. Accordingly, atomoxetine may be effective for HD and should be considered for future controlled trials [69].

Most research on the effectiveness of medications in HD has been conducted in patients in their midlife [70] and clinical trials examining psychotherapy outcomes for HD elderly patients are limited [71-73]. Research on CBT of late-life hoarding is restricted to case studies and open trials including older adults with compulsive hoarding [74, 75]. Case studies underlined the difficulties of handling late-life compulsive hoarding; yet, they should be taken with caution, since they do not take into consideration patient differences in medical status, neurocognitive conditions, insight, and treatment adherence. Although there is a lack of RCTs investigating CBT effectiveness in elderly HD (or compulsive

hoarding), two studies [76, 77] have conducted preliminary investigations in this population of the efficacy of the CBT protocol proposed by Frost and Hartl [78] and manualised in Steketee and Frost [79]. Another study [80] investigated a cognitive restructuring and exposure therapy for HD in older adults. Existing treatment approaches often target the cognitive and behavioural components of acquisition, difficulty organising, and avoidance of giving up saved items [12]. Despite the aforementioned challenges, current CBT techniques appear to be promising for HD treatment. These imply a gradual exposure to the task of discarding/throwing away (anxiety-provoking for HD patients), aiming to challenge distorted beliefs related to hoarding and to learn practical organizational strategies [12]. A multiple baseline experimental case study with a pilot version of the current CBT protocol showed significant improvement of clutter symptoms over 18 months [81]. A pilot case study focusing on individual and group treatment of compulsive hoarding showed similar results that lasted between 20 and 48 weeks. After almost one year, most patients showed improvement of symptoms, and they had much more free space to use, although supplementary work was still necessary for remaining clutter [82]. Also, OCD patients who described hoarding as their primary symptom showed significant improvement after a 6-week daily multimodal therapy including SSRIs, CBT based on Frost and Hartl's model [78], and psychosocial rehabilitation. Although HD patients showed less improvement than non-HD patients, their Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) scores at the end of treatment were significantly decreased [83].

Current CBT strategies for hoarding address the four deficits that are hypothesised to exist in hoarding, *i.e.*, information processing, beliefs about possessions, behavioural avoidance, and emotional attachment. These strategies typically last 6-12 months, and involve all parts of the house. An initial motivational interviewing module [84] may also be added, since delayed recognition and limited insight into hoarding-related issues have been encountered in this population [85], as well as a greater tendency of hoarding patients to refuse treatment or drop out of it [86]. CBT comprises emotional exposure modules for hoarding, which implies that patients categorise a hierarchy of items that are increasingly difficult for them to abandon (*e.g.*, newspapers, dress, equipment), bringing them at the session with the aim to sort and discard them [12]. Patients also use cognitive strategies in the different domains of hoarding, including acquisition, saving, and discarding. Treatment options in the context of psychotherapy involve both individual and group settings [87], and this may also extend to patients with animal hoarding [88]. A pilot study compared the outcome of CBT in six patients attending group treatment and one patient receiving individual treatment, all affected by compulsive hoarding. After 20 weekly-sessions of treatment, two-third of patients improved, especially in the domain of excessive acquisition, but none achieved full remission [82]. Future research may establish which hoarding-related variables may predict treatment outcomes. So far, worse outcomes have been linked to male gender, severe hoarding to lack of insight, social anxiety, and pathological personality aspects such as perfectionism [89].

Summarising, the pharmacological treatment of hoarding symptoms and HD did not change significantly after the nosographic split and few studies were dedicated to this new diagnosis. The interest on the effects of drugs in HD appears to be low; in fact, a PubMed search of “hoarding disorder”[title] on 3 January 2019 yielded 113 records, of which 26 were focused on psychotherapy and only four on pharmacotherapy. The difference emerges also in mixed reviews, where psychotherapy clearly outdoes pharmacotherapy in terms of performed studies [90, 91].

CONCLUSION

Six years after the official recognition of HD, it appears that psychopharmacological clinical practice has changed little since the times it was incorporated in OCD. No double-blind RCTs of drugs in HD are currently available and CBT and psychotherapy, in general, dominate the scene. We very much need RCTs of anti-ADHD and anti-OCD medications to be able to treat this difficult patient population. We also need to compare individual treatments with psychotherapeutic interventions, alone or in combination. The current picture is one of desolation. In fact, on ClinicalTrials.gov under the heading Hoarding Disorder there appear only 14 studies, just one using drugs, which has been concluded and has results, corresponding to our cited case series [69]; all other projected trials involve psychotherapy.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

This work has not been supported by any funding. All authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in, or financial conflict with the subject matter or materials discussed in the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

We gratefully acknowledge the contribution of the Librarians of the School of Medicine and Psychology of Sapienza University, Ms. Mimma Ariano, Ms. Felicia Proietti, Ms. Ales Casciaro, Ms. Teresa Pioreschi, and Ms. Susanna Rospo for rendering precious bibliographical material accessible, as well as our Secretary Lucilla Martinelli for her assistance during the writing of this manuscript.

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